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Review Article

Plant vs Animal Protein Sources: Evaluating Bioavailability and Cardiovascular Health Outcomes

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ABSTRACT

The nutrition debate surrounding plant-based and animal-based proteins has gone beyond simple nutritional sufficiency to one focused on improving long-term metabolic health and preventing disease. This review aims to compare the structural profiles, amino acid composition, and digestion kinetics of plant and animal proteins. Animal proteins typically have complete profiles of essential amino acids and high bioavailability. Plant proteins, on the other hand, are frequently found to be deficient in specific essential amino acids and contain anti-nutritional factors which are inhibitory to enzyme cleavage.

However, prospective cohort studies and clinical trials repeatedly show that replacing animal proteins with plant proteins decreases the risk of cardiovascular disease (CVD), improves lipid profiles and increases insulin sensitivity. This paper summarizes the biochemical mechanisms responsible for these observations, and discusses the interaction of different matrix components, including dietary fibre, phytosterols, saturated fatty acids and heme iron, with the gut microbiota and vascular endothelium, and their effect on cardiovascular outcomes.

Keywords*: Plant-Based Proteins; Animal-Based Proteins; Protein Bioavailability; Amino Acid Composition; Cardiovascular Health; Lipid Profile; Insulin Sensitivity; Gut Microbiota; Dietary Fibre; Heme Iron.*

INTRODUCTION

Proteins are crucial in the maintenance of the structure of the cell, as well as for the regulation of enzymatic reactions and the maintenance of skeletal muscle homeostasis. Traditional nutrition recommendations were mainly aimed at the prevention of deficiency states, and established minimum daily allowances as a function of the amount of crude protein consumed. With the current nutritional context in which more and more studies are focused on the effect of source of dietary protein on chronic diseases, especially cardiovascular disease (CVD), which is one of the main reasons for the large number of deaths worldwide (World Health Organization, 2024).

The different classification of plant and animal proteins is not just about where they come from but also about some basic differences in biochemical structures, yields of essential amino acids (EAA), and rates of digestion. Animal proteins have traditionally been considered "high quality" proteins or "complete" proteins, because the EAAs they provide are quite similar to those the human body needs. In contrast, plant proteins (legumes, cereal grains, nuts, seeds) are generally considered to be a "low-quality" protein because they contain limiting amino acids which can impede protein synthesis when consumed as a single component of a diet (Mariotti & Gardner, 2019).

Although some plant proteins have reduced standalone bioavailability, epidemiological evidence suggests that consumption of plant-rich diets is associated with lower cardiovascular mortality, better vascular reactivity, and better lipid metrics (Hu et al., 2020). This review will first outline the comparative biochemistry of plant and animal proteins, followed by a discussion of the physiological barriers that affect their bioavailability and then a description of the metabolic pathways by which the protein matrices can affect cardiovascular health.

Structural and Chemical Disparities in Protein Matrices

Amino Acid Profiling and Limiting Amino Acids

The primary structure, secondary structure and tertiary structure of proteins determines its nutritional value as they determine the amino acid profile of the protein source. Humans have nine amino acids that they cannot make de novo: histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine.

The amino acid composition of animal proteins closely resembles that of organs and tissues of human skeletal muscles. This means that they contain a high level of all 9 EAAs in one matrix.

Plant proteins, on the other hand, tend to be low in certain amino acids (EAAs) which are required in human diet in certain quantities:

Legumes (e.g. lentils, chickpeas, soybeans): Contain high levels of lysine and threonine and are generally deficient in SAA (methionine and cysteine) (Gorissen et al., 2018).

Cereal Grains (e.g. wheat, rice, oats): Have sufficient amount of methionine and cysteine, but are consistently deficient in lysine and threonine.

This is a complete EAA profile (Balanced match to human tissue) due to animal proteins.

Strategic dietary diversification (grains with legumes, for example) will be necessary to achieve a full complementary amino acid pool throughout a day's intake due to this structural variance.

The Leucine Trigger and Satiety Peptides
Amino acids are signaling molecules in addition to their basic repair function. Leucine is central to metabolic signaling through activation of mammalian target of rapamycin complex 1 (mTORC1) pathway and activation of myofibrillar protein synthesis (MPS) (Norton & Layman, 2006).

The leucine content of animal proteins is on average 9% to 11%, in contrast with plant proteins, which on average have 6% to 8% leucine (Gorissen et al., 2018). The leucine trigger—concentrations reached by the leucine in the cell that are required to achieve maximum levels of MPS—is generally lower for total animal protein intake than for total plant protein intake.

Furthermore, animal and plant proteins activate distinct peripheral satiety peptide (e.g., peptide YY [PYY] and glucagon-like peptide-1 [GLP-1]) secretion which is mediated by distinct activation of calcium-sensing receptors in the distal gut (reger et al., 2021).

Methodologies and Evaluation of Bioavailability
Bioavailability is defined as the fraction of ingested amino acids that are digested, enter the enterocyte wall, and are delivered to the metabolic pathways in the systemic circulation.

PDCAAS vs. DIAAS Metrics
The Protein Digestibility-Corrected Amino Acid Score (PDCAAS) has been used to measure the quality of protein for decades. The PDCAAS of a test protein is the product of the amino acid score of the test protein and its true digestibility in the faeces of rodents (FAO/WHO, 1991). There are, however, some inherent limitations to PDCAAS: First, it is based on fecal digestibility, which may be influenced by the amino acid metabolism of the colon microflora; second, it reduces higher values to the maximum score of 1.0 (or 100%).

The FAO (2013) have developed the Digestible Indispensable Amino Acid Score (DIAAS) to overcome these drawbacks. The methodological improvements of DIAAS are:

1. **Ileal Digestibility:** Ileal Digestibility is a measure of disappearance of amino acids at the terminal ileum in the absence of any confounding effect caused by bacterial fermentation in the large intestine.
2. **Individual Values**: It determines each indispensable amino acid digestibility individually and not using an average crude protein value.
3. **No Truncation:** It does not truncate scores, so it can be used to directly assess high quality protein matrices.

Protein Source	PDCAAS Score	DIAAS Score	Limiting Amino Acid
Milk Protein Isolate	1.00	1.18	None
Egg White Powder	1.00	1.13	None
Soy Protein Isolate	1.00	0.90	Methionine
Pea Protein Concentrate	0.89	0.70	Methionine
Whole Wheat Flour	0.45	0.40	Lysine

Anti-Nutritional Factors and Protein Structure Interferences

Anti-nutritional factors occurring together in the plant cell wall matrix are a common cause of the lower DIAAS values of plant proteins. These compounds do not allow the plant to be eaten by environmental pests, but they are very harmful to human digestion:

- Phytates (Phytic Acid): which can form insoluble chelation complexes with dietary essential cations (Ca^{2+}, Zn^{2+}, Fe^{2+}) and bind directly to basic amino acid residues (lysine, arginine, histidine), thereby lowering protein solubility and competitively inhibiting pepsin activity (Schlemmer et al., 2009).
- Tannins and Polyphenols: Make hydrophobic cross-links with dietary proteins and endogenous digestive enzymes (e.g. trypsin, chymotrypsin) that makes the complex insoluble and interferes with luminal digestion.
- Trypsin Inhibitors (Kunitz and Bowman-Birk inhibitors): These proteins are found in raw legumes, and inhibit the activity of pancreatic trypsin and chymotrypsin by competitive binding and result in compensatory pancreatic hypertrophy (Gilani et al., 2012).

Thermal processing, fermentation, germination and chemical isolation are modern food processing technologies that can reduce the level of these anti-nutritional factors and increase the DIAAS profile of isolated plant proteins to a level closer to animal proteins.

Cardiovascular Health Outcomes: Epidemiological Evidence

The results of large-scale nutritional epidemiology consistently show opposing cardiovascular health patterns with plant versus animal protein consumption.

Cardiovascular and All-Cause Mortality Tracking

A study of more than 130,000 women for approximately 30 years, known as the Nurses' Health Study and the Health Professionals Follow-up Study, showed that a particularly high consumption of animal protein was associated with an increase in cardiovascular deaths (Song et al., 2016). This link was strongest in people who had one or more lifestyle risk factor (smoking, physical inactivity, overweight or obesity).

On the other hand, high consumption of plant protein was inversely related to all-cause and cardiovascular mortality. Iso-caloric substitution models show that replacing animal protein with plant protein by 3% of daily energy intake is related to 12% reduction in cardiovascular mortality risk (Song et al., 2016).

Ischemic Heart Disease and Stroke Associations

The Profiles of Risk (PURE) study and a set of rigorous meta-analyses also showed that there are significant differences in the risk profile across animal protein (Dehghan et al., 2017). There is a strong positive correlation between processed red meats (e.g., bacon, sausage, deli meats) and ischemic heart disease and ischemic stroke.

Unprocessed red meat has poor and inconsistent relationships, while white meat (poultry) and fish tend to have either neutral or inverse relationships with acute cardiovascular events (Zhong et al., 2020). The case for plant proteins from nuts and legumes and decreased risk of atherothrombotic disease is consistent in various geographical populations.

Biochemical and Metabolic Mechanisms

Serum Lipid and Lipoprotein Regulation

Changes in serum lipids profiles are a major contributor to the association of protein sources and cardiovascular risk. Substituting animal protein for plant protein has been demonstrated to lower LDL-C (low-density lipoprotein cholesterol), non-HDL-C (non-high-density lipoprotein cholesterol) and apolipoprotein B (ApoB) which is the major structural protein of atherogenic lipid particles (V良et al., 2017).

The arginine/lysine ratio of the protein consumed is a factor of this lipid lowering effect. The protein of plant origin with a high ratio of arginine to lysine, such as soy and pea isolates. Arginine increases glucagon secretion compared to insulin's, which lowers the insulin to glucagon ratio of the portal vein.

This hormonal change appears to downregulate the expression of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the enzyme that reduces cholesterol in the liver, and to upregulate the expression of the LDL receptor, the protein that removes atherogenic particles from the circulation (Sirtori et al., 1995).

Endothelial Function, Nitric Oxide Synthesis, and Blood Pressure

Endothelial dysfunction is a key early and crucial event in the initiation of atherosclerosis. Plant proteins provide a rich source of the obligate substrate of endothelial nitric oxide synthase (eNOS), L-arginine (Moncada & Higgs, 1993). Increases in eNOS activity increase the production of nitric oxide (NO), which diffuses into vascular smooth muscle cells and activates guanylyl cyclase, leading to vasodilation.

Increased NO levels result in better FMD and decreases systemic arterial blood pressure, thus decreasing mechanical strain on the vascular wall (Appel et al., 2005). In addition, plant-based bioactive peptides are frequently endogenous angiotensin-converting enzyme (ACE) inhibitors, which are aiding further to reduce vasoconstrictive pathways.

Systemic Inflammatory Cascades and "Inflammaging"

Plaque build-up occurs when there is a chronic low-grade inflammation in the blood vessels, which eventually leads to plaque rupture. The protein profiles of different diets have been shown to influence biomarkers of inflammation such as high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α).

Processed animal proteins are associated with higher levels of circulating Hs-CRP, probably due to the high proportion of saturated fat and advanced glycation end-products (AGEs) produced during high-temperature meat cooking (Lopez-Garcia et al., 2005).

Plant protein matrices, on the other hand, are rich in antioxidant polyphenols, sulfur-containing compounds, and other nutrients which suppress the production of pro-inflammatory cytokines in the vascular endothelium via the inhibition of nuclear factor-kappa B (NF-κB) transcription pathways.

Co-Ingested Matrix Elements: The "Package" Effect
Proteins are not eaten in isolation in the real diet; they are consumed as part of a diet matrix of nutrients and bioactive compounds. This "package" effect can induce metabolic effects that are greater than the properties of the individual amino acids.

Saturated Fatty Acids versus Polyunsaturated Fatty Acids and Phytosterols
Animal protein packages are often high in saturated fatty acids (SFAs), such as palmitic and myristic acids, especially those from ruminant sources. SFAs decrease hepatic LDL receptor expression, which is associated with an increase in circulating levels of atherogenic lipids (Mensink et al., 2003).

Plant protein packages, on the other hand, are rich in mono- and polyunsaturated fatty acids (PUFAs) and also include phytosterols that have a unique structure such as beta-sitosterol. Phytosterols competitively inhibit the intestinal absorption of dietary and biliary cholesterol in the intestinal lumen by inhibiting the Niemann-Pick C1-Like 1 (NPC1L1) transporter (Plat & Mensink, 2005).

Heme Iron, Oxidative Stress, and Lipid Peroxidation
Heme iron is a major source of the animal protein, and particularly red meat. Heme iron is highly bioavailable for erythropoiesis but excess heme iron can cause cardiovascular complications. Free heme iron can assume part of the Fenton reaction, which happens to be a reaction amongst hydrogen peroxide and free heme iron generating highly damaging hydroxyl radicals ($\cdot OH$) (Aruoma et al., 1987).

Within the arterial intima these radicals trigger the oxidation of low density lipoproteins (oxLDL). Macrophages have scavenger receptors that quickly phagocytose oxLDL particles, leading to their foam cell formation and promotion of fatty streak formation. Plant proteins are proteins containing non-heme iron which is not as readily involved in these oxidative cascades.

Dietary Fiber and Short-Chain Fatty Acids (SCFAs)
Plant proteins are naturally associated with complex carbohydrates (soluble and insoluble fibres, e.g., beta-glucan, pectin, cellulose). These fibers are not broken down by the enzymes in the intestine, and pass into the cecum and colon. There they are fermented by some types of bacteria called saccharolytic bacteria to produce short-chain fatty acids (SCFAs), mainly acetate, propionate and butyrate (Cummings et al., 1987).

Propionate enters as a portal vein metabolite and enters the liver to inhibit acetyl-CoA carboxylase, which decreases de novo lipogenesis. Butyrate maintains the integrity of the intestinal barrier and prevents the leakage of pro-inflammatory lipopolysaccharides (LPS) into the blood stream, thus reducing inflammation that promotes atherosclerosis.

The Gut Microbiome Axis and Metabolite Generation
The relationship between dietary proteins and the gut microbiome produces certain metabolites that have protective or harmful effects on the cardiovascular system.

The TMAO Pathway
Animal proteins are very rich in choline, carnitine and betaine. These compounds are metabolized in the distal gut to the volatile gas trimethylamine (TMA) by particular taxons of the gut microbiota (e.g., Firmicutes and Proteobacteria) (Wang et al., 2011). The TMA is absorbed into the portal circulation and carried to the liver, where it is converted to trimethylamine N-oxide (TMAO) by flavin containing monooxygenase 3 (FMO3).

TMAO is a known pro-atherogenic metabolite which regulates cholesterol metabolism, stifles reverse cholesterol transport via macrophage scavenger pathways, and stimulates the NLRP3 inflammasome in endothelial cells leading to vascular calcification (Tang et al., 2013). Plant-based eating is missing these dense carnitine structures, and eating these foods encourages a microbiome profile which results in low levels of TMA.

Uremic Toxins and Tryptophan Metabolites
High meat, protein, diets provide abundant amounts of aromatic amino acids (tryosine, phenylalanine, tryptophan) to the distal colon where anaerobic bacterial fermentation changes toward proteolytic pathways. During this fermentation, uremic retention solutes such as indoxyl sulfate and p-cresol sulfate are produced (Vanholder et al., 2014). They may circulate and

cause endothelial cell microparticle release, oxidative stress in vascular smooth muscle, and promote cardiorenal syndrome and arterial stiffness.

Clinical Considerations and Public Health Strategies

The translation of biochemical/epidemiological data to clinical practice must take into account nutritional needs and the risk of chronic disease.

Optimizing Muscle Preservation and Cardiovascular Safety

One of the major concerns for full conversion to plant proteins is the worry about inadequate retention of muscle mass, especially in the elderly population at risk for sarcopenia or in athletes with a high demand for muscle mass. Since the independent DIAAS value and leucine content of plant proteins is lower, clinical strategies should involve protein blending and high dosage:

- **Dose Escalation:** Higher absolute doses of a plant protein source (e.g. 35–40 g pea protein isolate vs. 25 g whey protein) can also produce the same amount of leucine absorbed and protein degradation rate of MPS (Gorissen et al., 2018).
- **Amino Acid Supplementation:** The use of crystalline amino acids, such as synthetic L-lysine or L-methionine, to enrich plant-derived protein products may help to enhance the overall DIAAS profile without adding extra caloric load.

Comprehensive Food Processing and Novel Plant Protein Isolates

There are advanced plant protein isolates being developed by modern food industry such as texturized vegetable protein, mycoproteins and microalgae protein extraction. The products have good DIAAS characteristics and reduced environmental impact, however, they need to be monitored for overall preservative and sodium levels.

Ultra-processed substitutes to meat can have a high sodium content, as the salt is included to maintain the desired texture and taste. This may undo some endothelial protection by increasing hydrostatic blood pressure in salt-sensitive persons.

CONCLUSION

A comparison of plant and animal protein sources shows a clear dichotomy between short-term nutritional bioavailability and long-term cardiovascular consequences. Animal proteins have complete and highly digestible essential amino acid profile suitable for good musculoskeletal development. Their overall nutrient profile, however, can include higher levels of saturated fats, heme iron, and pro-inflammatory metabolites such as TMAO, which can lead to endothelial injury, lipid deposition, and increased atherogenesis.

In contrast, diet of plant proteins is limited by limiting components such as amino acids and anti-nutrients whereby intake is correlated with better outcomes for cardiovascular health. This protection is attributed to high arginine/lysine ratio for optimal lipid metabolism, enhanced nitric oxide synthesis from eNOS and an abundance of fiber, phytosterols, and polyphenols, which promotes a healthy gut microbiome profile and lower systemic inflammation.

The clinical evidence suggests that a dietary pattern focusing on protein in legumes, whole grain foods, nuts, and seeds is more beneficial for the cardiovascular health span. If animal proteins are incorporated, low fat dairy, poultry and seafood high in omega-3's can reduce the dangers of processed and red meat matrices.

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